

Serial No. 10/246,581
Amendment Dated 01/25/2005
Reply to Office Action Dated 08/25/2004

REMARKS/ARGUMENTS

Claims 1-27 are pending and currently under examination. The specification has been amended to update the cross-reference to related applications, and to clarify references to resources available on the internet, no new matter has been introduced by any of the amendments. Claims 5 and 15 have been amended, no new matter has been introduced by these amendments to the claims.

Information Disclosure Statement:

Applicant notes with thanks the receipt of an initialed copy of the Information Disclosure Statement submitted March 8, 2004.

Specification:

The paragraph beginning on page 1, line 7 has been amended to update the cross-reference to related applications, and recites that U.S. Application Serial No. 09/589,510 filed June 7, 2000, issued March 16, 2004 as U.S. Patent 6,706,949. No new matter has been added by this amendment.

The Examiner asserted that the specification contained embedded hyperlinks to an internet address. Applicant respectfully disagrees, since the text does not include "http\\", the text is not an embedded hyperlink, and cannot be directly used as an active hotlink to the recited internet address. However, in order to expedite prosecution, Applicant has submitted the following amendments to clarify the text.

The paragraph beginning on page 19, line 26 has been amended to recite "Software for performing BLAST analyses is publicly available, e.g., through the National Center for Biotechnology Information website (www.ncbi.nlm.nih.gov/)".

The paragraph beginning on page 69, line 16 has been amended to recite "Gene identities were determined by conducting BLAST (Basic Local Alignment

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Search Tool; Altschul, S. F., et al., (1990) J. Mol. Biol. 215:403-410; see also NCBI website www.ncbi.nlm.nih.gov/BLAST/

Rejections under 35 U.S.C. §101 – Non-Statutory Subject Matter:

Claims 5 and 15-16 were rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The Action asserts that the claims encompass naturally occurring cells.

In order to expedite prosecution, claims 5 and 15 have been amended to replace "comprising" with "transformed with" as recommended by the Examiner, thereby obviating the rejection of claims 5, 15, and dependent claim 16 under 35 U.S.C. §101.

Rejections under 35 U.S.C. §112, 1st Paragraph – Enablement:

Claims 1-27 were rejected under 35 U.S.C. §112, 1st paragraph as not being enabled by the specification.

The Action asserts that the specification does not enable one of skill in the art to make and used an isolated polynucleotide which encoding a polypeptide having RuvB activity, wherein the polynucleotide has 80%, 85%, and 90% sequence identity with the disclosed sequences. The Action concludes:

- the Applicant must provide sufficient guidance to obtain all nucleic acid sequences encompassed by the claims (emphasis added); and
- the start of the prior art teaches that sequence identity alone cannot be used to determine the function of a protein/DNA, citing:
 - Lazar *et al.* (MCB 1988 8:1247-1257); and
 - Amgen Inc. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021 and 1027 (Fed. Cir. 1991), concluding that a gene must be defined by its physical and chemical properties (1021), and disclosure of a few sequences did not enable broad claims (1027).

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Applicants respectfully disagree. As stated in MPEP 2164.01 (page 2100-185, 1st col.) "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation" (*United States v Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d, 1217, 1223 (Fed. Cir. 1988)). Applicant has provided sufficient guidance by disclosing four full-length RuvB sequences from corn, the first identified plant RuvB homologues, and further describing homologues having percent sequence identity (e.g., page 18, line 15 – page 24, line 7), codon degeneracy (e.g., page 8, lines 10-29), amino acid substitutions (e.g., page 6, line 30 – page 8, line 8), nucleic acid hybridization (e.g., page 16, line 5 – page 17, line 27; and page 30, lines 1-22), and further demonstrating conserved RuvB domains (see Example 4, pages 70-71; and **Appendix C** PileUp and HmmerPfam analyses). Other RuvB homologues were known in the art at the time of filing as shown in **Appendix B**. Assays for RuvB were known in the art at the time of filing. For example, Qui, *et al.* (J. Biol. Chem. 273(43):27786-27798 1998, Ref. A16 in IDS submitted 3/8/04) describe several assays for RuvB including gels and immunoblots (page 27787, col. 1, paragraph 4; and Fig. 3, page 27791), and RNA polymerase II holoenzyme binding (page 27790, col. 1, paragraph 4), and complementation tests in yeast (page 27790, col. 2, 3rd paragraph). In their study of the RuvB homologue TIP49, Makino, *et al.* (Biochem. Biophys. Res. Comm. 245:819-823 1998, Ref. A12 in IDS submitted 3/8/04) describe ELISA and immunoblotting assays (page 820, col. 2, paragraphs 5 and 6; and Fig. 3, page 822). Kishimoto, *et al.* (EP 0 926 157 A1, Ref A3 in IDS submitted 3/8/04) further disclosed ATPase and helicase assays for TIP49 (Examples 7-9, page 16, paragraph 0095 page 17, paragraph 0101). Therefore, one of skill in the art, using Applicant's disclosure coupled with the knowledge in the art, could make and use RuvB polynucleotides having 80%, 85%, and 90% sequence identity without undue experimentation.

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The sequence conservation of TIP49 homologues is noted by Kurokawa *et al.* (Appendix A, DNA Sequence 10:37-42 1999), which concludes that this family of sequences demonstrates a highly conserved gene among organisms (Abstract, page 37), and demonstrates that one of skill in the art does believe that sequence homology is predictive of function, contrary to the conclusion drawn from the Lazar reference. Further, one of skill in the art could use a multiple sequence alignment, similar to that presented in Appendix C, to note highly conserved vs. not well conserved residues, and to predict residues and/or regions likely to tolerate amino acid substitutions and further predict which amino acid substitutions that would be tolerated, based on the conserved residues and substitutions seen in the alignment of the homologues. Examiner is reminded that the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *In re Wands*, 8 USPQ2d 1400 (Fed Cir 1988). Furthermore, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *Id.* See also *Johns Hopkins University v. Cellpro*, 931 F. Supp. 303, 324 (D. Del. 1996), *aff'd in part, vacated in part, & remanded*, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998) ("The specification need only enable one mode of making the claimed invention.").

The disclosed plant sequences, coupled with other known RuvB homologues and the availability of routine assays for functional RuvB, polynucleotides having 80%, 85%, and 90% sequence identity could be made and used one of skill in the art, at the time of filing, without undue experimentation. Therefore the rejection of claims 1-27 for lack of enablement under 35 U.S.C. §112, 1st paragraph should be withdrawn.

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Rejections under 35 U.S.C. §112, 1st Paragraph – Written Description:

Claims 1-27 were rejected under 35 U.S.C. §112, 1st paragraph as not having written description support in the specification.

The Action asserts that the specification does not reasonably convey to one of skill in the art that the inventors had, at the time of filing, possession of an isolated polynucleotide which encoding a polypeptide having RuvB activity, wherein the polynucleotide has 80%, 85%, and 90% sequence identity with the disclosed sequences. The Action concludes that the Applicant must describe the composition and structure of all nucleic acid sequences encompassed by the claims (emphasis added).

Applicants respectfully disagree. Every species encompassed by the claimed invention need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga*, 845 F.2d 993, 6 USPQ2d 1709 (Fed. Cir. 1988). In fact, the Examiner is reminded that information that is well known in the art need not be described in detail in the specification. Evidence that functional RuvB sequences and homologues were known in the art at the time of filing is provided in **Appendix B** which presents the results of a keyword (RuvB or TIP49) search of the nucleotide database at NCBI, which was then further limited to the annotated hits deposited in the database on or before Applicant's priority date of July 16, 1999. Further, Applicant has disclosed four full-length RuvB sequences from corn, the first identified plant RuvB homologues, and further described homologues having percent sequence identity (e.g., page 18, line 15 – page 24, line 7), codon degeneracy (e.g., page 8, lines 10-29), amino acid substitutions (e.g., page 6, line 30 – page 8, line 8), nucleic acid hybridization (e.g., page 16, line 5 – page 17, line 27; and page 30, lines 1-22), and further demonstrated conserved RuvB domains (see Example 4, pages 70-71). Assays for RuvB were known in the art at the time of filing. For example, Qui, *et al.* (J. Biol. Chem. 273(43):27786-27798 1998, Ref. A16 in IDS submitted 3/8/04) describe

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several assays for RuvB including gels and immunoblots (page 27787, col. 1, paragraph 4; and Fig. 3, page 27791), and RNA polymerase II holoenzyme binding (page 27790, col. 1, paragraph 4), and complementation tests in yeast (page 27790, col. 2, 3rd paragraph). In their study of the RuvB homologue TIP49, Makino, *et al.* (Biochem. Biophys. Res. Comm. 245:819-823 1998, Ref. A12 in IDS submitted 3/8/04) describe ELISA and immunoblotting assays (page 820, col. 2, paragraphs 5 and 6; and Fig. 3, page 822). Kishimoto, *et al.* (EP 0 926 157 A1, Ref A3 in IDS submitted 3/8/04) further disclosed ATPase and helicase assays for TIP49 (Examples 7-9, page 16, paragraph 0095 page 17, paragraph 0101). The sequence conservation of TIP49 homologues is noted by Kurokawa *et al.* (Appendix A, DNA Sequence 10:37-42 1999), which concludes that this family of sequences demonstrates a highly conserved gene among organisms (Abstract, page 37), and demonstrates, as noted above, that one of skill in the art does believe that sequence homology is predictive of function.

The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims."). The written description requirement does not require the literal recitation of each and every species, as the current Action appears to conclude. One of skill in the art can immediately envision the product claimed from the disclosure in the current application, therefore the rejection of claims 1-27 for lack of written description under 35 U.S.C. §112, 1st paragraph should be withdrawn.

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CONCLUSION

In light of the foregoing remarks and amendments, it is believed that claims 1-27 are in condition for allowance. Withdrawal of the outstanding rejections and allowance of all of the remaining claims is respectfully requested.

Respectfully submitted,



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